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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,497	07/01/2003	Douglas Charles Hanson	ABX-PF1 DIV1	3552

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EXAMINER	
OUSPENSKI, ILIA I	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/612,497	HANSON ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2004 and 18 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *105 - 176* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *105 - 176* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/12/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 01/18/2005, is acknowledged.

Claims 1 – 31 have been cancelled.

Claims 32 – 104 have been cancelled previously.

Claims 105 – 176 have been added.

Claims 105 – 176 are pending.

2. Applicant's election of claims drawn to antibody 4.13.1 in reply filed 11/03/2004 is acknowledged; however, Applicant's subsequent cancellation of all claims drawn to said antibody has rendered the election moot. Applicant's submission of new claims 105 – 176 is interpreted as an election of a newly presented Invention, drawn to a method for producing human monoclonal antibodies to CTLA-4.

Claims 105 – 176 are under consideration in the instant application.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth herein.

Upon review of the instant application, it is noted that the sequences disclosed at least on page 57, lines 24 – 31, page 59, line 29, pages 66 – 67, and in Figures 3 – 9 *are not accompanied by SEQ ID Numbers*. The sequences disclosed in Figures must be accompanied by SEQ ID Numbers either in the Figure itself of in the corresponding Brief Description of the Drawings.

Applicant is reminded of the sequence rules which require a submission for all sequences of more than 9 nucleotides or 3 amino acids (see 37 CFR 1.821-1.825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules. Applicant is reminded to amend the specification and the claims accordingly.

Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) in response to this Office Action.

4. Applicant's claim for domestic priority under 35 U.S.C. 119(e) and 120 is acknowledged. The priority applications 09/472,087 and 60/113,647 appear to provide adequate support under 35 U.S.C. 112 for subject matter claimed in the instant application.

The specification on page 1, first paragraph should be amended to reflect the status of the priority application USSN 09/472,087.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

6. Applicant's IDS, filed 02/12/2004, is acknowledged, and has been considered.

Applicant's amendment notes that the references have been submitted with the priority application 09/472,087. However, reference identified as "RE 35,500; Rhodes" could not be located in the file of application 09/472,087, and has been crossed out. Applicant is invited to resubmit this reference to complete the instant file.

It is noted that where only a part of the reference has been provided, only the pages indicated in the IDS have been considered (e.g. Dayhoff, 1976).

Publication dates has been added to references "Leukocyte Typing VI" and "Mandal et al."

7. The use of trademarks has been noted in this application (e.g. Lipofectin™ on page 47). Each letter of the trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

8. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP §608.01(o). Correction of the following is required:

The specification fails to provide proper antecedent basis for the limitation of "hybridoma cell line deposited under ATCC accession number PTA-5166" in claims 105 and 138. Applicant is required to amend the specification to provide antecedent basis for said limitation. Alternatively, Applicant is invited to identify the written support for the claimed limitation.

9. The disclosure is objected to because of the following informalities: the specification includes apparent spelling errors.

A. The specification discloses apparently distinct cell lines "NSO_0" (page 49 line 19) and "NSO" (page 68 line 5), while claims 113, 124, 135, 146, and 156 include a recitation of an "NS0" cell line.

Appropriate correction AND clarification is required. Alternatively, claims 113, 124, 135, 146, and 156 are subject to New Matter rejection, as detailed below.

B. The specification contains other apparent spelling errors, such as, for example, in the word "sythetase" on page 49, line 31. Appropriate correction is required.

Applicant is requested to proofread the specification and correct any other possible errors.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 127 – 137 and 164 – 171 are rejected under **35 U.S.C. 112, first paragraph**, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a New Matter rejection.*

Applicant's amendment asserts that no New Matter has been added and points to the specification at pages 48 – 51 for support for these claims. However, the specification does not appear to provide an adequate written description of the limitations of "SEQ ID NO:1 without the signal sequence," or "SEQ ID NO:14 without the signal sequence."

The specification discloses on page 70, lines 25 – 26, that the signal peptide sequences are indicated in bold in Figure 1, which shows, among others, the polypeptides of SEQ ID NOS:1 and 14. However, this is not deemed as sufficient

support under the description requirement of the first paragraph of 35 U.S.C. 112 for the limitations of "SEQ ID NO:1 (or 14) without the signal sequence."

The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the New Matter in the response to this Office Action. Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

13. Claims 113, 124, 135, 146, and 156 are rejected under **35 U.S.C. 112, first paragraph**, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a New Matter rejection.*

The newly added claims 113, 124, 135, 146, and 156 recite a limitation of an "NS0" cell line. However, the specification does not appear to provide an adequate written description of this limitation.

As noted in section 9 above, the specification discloses apparently distinct cell lines "NSO_0" (page 49 line 19) and "NSO" (page 68 line 5). However, this is not deemed as sufficient support under the description requirement of the first paragraph of 35 U.S.C. 112 for the limitation of "NS0" cell line.

The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the New Matter in the response to this Office Action. Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

If Applicant regards the variations in cell line names as spelling errors, and provides appropriate explanation and correction, this rejection will be withdrawn.

14. Claims 105 – 115 and 138 – 147 are rejected under **35 U.S.C. 112, first paragraph**, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the hybridoma cell line deposited under ATCC accession number PTA-5166 is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, a deposit of the hybridoma, which produces this antibody, may satisfy first paragraph. See 37 CFR 1.801-1.809.

If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the hybridoma has been deposited under the Budapest

Treaty and that the hybridoma will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample *or for the enforceable life of the patent whichever is longer.* See 37 CFR 1.806. If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

If the deposit(s) was/were made after the effective filing date of the application for a patent in the United States, a verified statement is required from a person in a position to corroborate that the hybridoma described in the specification as filed are the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Further, amendment of the specification to disclose the date of deposit and the complete name and address of the depository (ATCC.10801 University Boulevard, Manassas, VA 20110-2209) is required as set forth in 37 C.F.R. 1.809(d).

Applicant's submission of a copy of Declaration by Vahe Bedian filed 07/07/2003 in parent application 09/472,087, relating to deposited biological material, is acknowledged. However, this declaration is not deemed sufficient to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons detailed below.

The Examiner also acknowledges that a statement by Jane Gunnison, Applicant's Representative, affirming that the deposit of biological material has been made under the terms of the Budapest Treaty, and that all restriction of the availability to the public of deposited material will be irrevocably removed upon the granting of the patent, has been filed in priority application 09/472,087 on 07/07/2003. Further, a copy of ATCC deposit receipt of biological materials has been provided in said application. Copies of these two documents have been made of record in the instant application.

However, the record remains unclear with regard to the identity of the deposited material as it relates to the identity of the biological material claimed in the instant application.

The instant claims are directed to a hybridoma cell line deposited under ATCC accession number PTA-5166, and to an antibody of SEQ ID NOS:1 and 14. The instant specification discloses in Figure 1 that SEQ ID NOS:1 and 14 correspond to an antibody designated as "4.1.1."

Declaration by Vahe Bedian is directed to an antibody designated as "PF1-4.1.1.1," and asserts that this antibody comprises SEQ ID NOS:53 and 56. The Statement by Jane Gunnison asserts that cell line "PF1-4.1.1.1" has been deposited with ATCC under deposit number PTA-5166, and the ATCC deposit receipt shows that cell line (PF1-4.1.1.1): LN 15887 has been designated as PTA-5166.

Therefore, the identity of the cell line deposited with ATCC under accession number PTA-5166 remains unclear. Applicant is invited to submit a verified statement from a person in a position to corroborate the fact, to clarify the relationship between cell lines designated as "4.1.1" in the instant application and "PF1-4.1.1.1" in the Declaration by Vahe Bedian, statement by Jane Gunnison, and ATCC deposit receipt.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 105 – 110 and 112 are rejected under **35 U.S.C. 102(b)** as being anticipated by Kuchroo et al. (US Patent 6,207,156; or record, see entire document).

Kuchroo et al. teach humanized monoclonal antibodies that specifically bind to human CTLA-4 (see entire document, in particular, e.g. column 6 last paragraph and column 2 second paragraph), and define humanized monoclonal antibodies as *human* monoclonal antibodies (e.g. column 7 first paragraph and last paragraph). Kuchroo et al. further teach antibodies which inhibit binding of human CTLA-4 to B7 molecules, including B7-1 and B7-2 (e.g. column 5 second paragraph, column 2 second paragraph, and column 21, Example 2), and have therapeutic potential in humans (see entire document, in particular e.g. columns 16 – 17, bridging paragraph).

Kuchroo et al. also teach that anti-CTLA-4 humanized monoclonal antibodies can be produced by "any method known in the art" (column 7 first paragraph), such as transforming a mammalian cell line with vectors encoding heavy and light chains of the antibody and culturing it "under conditions known to those of skill in the art to produce the humanized antibody" (column 7 second paragraph). The examples of cells in which the antibodies can be produced include CHO cells (columns 15 – 16 bridging paragraph). The step of culturing the antibody producing cells is followed by the step of harvesting culture media (column 20 last paragraph), i.e. recovering the antibody.

Given that both the antibodies taught by Kuchroo et al. and the instantly claimed antibody produced by PTA-5166 inhibit binding of human CTLA-4 to B7-1 and B7-2, it is

inherent that the antibodies taught by Kuchroo et al. would compete with the antibody produced by PTA-5166 for binding to human CTLA-4. Even as the reference is silent as to the specific IC_{50} values, since the antibodies have therapeutic potential, it is expected that their functional properties would be the same as of the instantly claimed antibodies.

The reference teachings thus anticipate the claimed invention.

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 105, 111, 113, and 115 are rejected under **35 U.S.C. 103(a)** as being unpatentable over Kuchroo et al. (US Patent 6,207,156; or record, see entire document) in view of European Patents 0 216 846 and 0 256 055 (of record, see entire documents) and Kucherlapati et al. (US Patent 5,939,598; of record, see entire document).

Kuchroo et al. have been discussed supra and teach methods of producing human monoclonal antibodies to CTLA-4 with functional characteristics recited in the instant claim 105. Kuchroo et al. further teach that such antibodies have therapeutic potential in humans (see entire document, in particular e.g. columns 16 – 17, bridging paragraph).

Kuchroo et al. do not specifically exemplify the methods of producing said antibodies employing a glutamine synthetase expression system, a method of producing said antibodies in NS0 cells, or a method producing such antibodies wherein the encoding polynucleotides were generated in a mouse whose genome comprises human immunoglobulin genes.

European Patent 0 256 055 teaches a method of expressing a protein of interest eukaryotic cells employing a glutamine synthetase expression system (see entire document, in particular, e.g. page 3 lines 15 – 30), and reviews a number of advantages of this expression system over other systems (e.g. pages 2 – 3).

European Patent 0 216 846 teaches a method of expressing a protein of interest, such as an immunoglobulin in myeloma cell lines, and in particular, in NS0 cells (see entire document, in particular, page 3 first paragraph and page 6 first paragraph), and reviews a number of advantages of this expression system over other systems (e.g. page 2).

Kucherlapati et al. teach methods of producing antibodies in mice whose genome comprises human immunoglobulin genes (see entire document, in particular e.g. Summary of the Invention in column 2), and reviews the advantages of such methods (e.g. Introduction in columns 1 – 2).

Thus it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Kuchroo et al. with the teachings of

European Patents 0 216 846 and 0 256 055 and Kucherlapati et al. to arrive at the instant claimed invention. Ordinary artisan would have been motivated to do so, given the art-recognized therapeutic applications of anti-CTLA-4 antibodies, as noted e.g. by Kuchroo et al., and the advantages of the respective expression systems, reviewed in the respective European Patents and in Kucherlapati et al. Furthermore, the ordinary artisan would have had a reasonable expectation of success, given the examples provided in the references.

Independent claim 105 is included, because it encompasses the limitations of claims 111, 113, and 115.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

19. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 105 – 176 are provisionally rejected under the judicially created doctrine of **obviousness-type double patenting** as being unpatentable over claims 1 – 4, 9 – 11, 16 – 17, and 20 of copending Application USSN 10/776,649, as evidenced by the instant disclosure on page 69 and Figure 1, and by the statement by Jane Gunnison (filed 07/07/2003 in priority application 09/472,087), in view of Kucherlapati et al. (US Patent 5,939,598; of record, see entire document), Kuchroo et al. (US Patent 6,207,156; or record, see entire document), and European Patents 0 216 846 and 0 256 055 (of record, see entire documents).

Claims 1 – 4, 9 – 11, 16 – 17, and 20 of copending Application No. 10/776,649 are directed to an antibody that is capable of binding to CTLA-4, comprising a heavy chain encoded by a human V_H3-33 family gene, or comprising SEQ ID NO:1, or SEQ ID NO:14, or competing with antibody 4.1.1.

The instant disclosure specifies on page 69 that clone 4.1.1 comprises a heavy chain encoded by gene DP-50, also referred to as a V_H3-33 family gene (Table II and line 8). Figure 1 specifies that clone 4.1.1 expresses an antibody of SEQ ID NO:1 and 14.

Statement by Jane Gunnison, filed 07/07/2003 in priority application 09/472,087, affirms that clone PF1-4.1.1.1 has been deposited with ATCC under deposit number PTA-5166. It is noted that although the record is unclear with regard to the relationship between clones PF1-4.1.1.1 and 4.1.1, it is assumed for the examination purposes that the two designations refer to the same biological material, pending Applicant's clarification (see section 14 supra).

Thus, claims in the copending '649 application are directed to the same antibodies as the instant claims. Therefore all functional limitations recited in the instant claims would be inherent properties of the antibodies claimed in the '649 application.

Application No. 10/776,649 does not claim methods of producing said antibodies.

However, an ordinary artisan at the time the invention was made would immediately envisage such methods, as evidenced by the references. For example, Kucherlapati et al., Kuchroo et al., and European Patents 0 216 846 and 0 256 055 have been discussed supra, and teach the various methods of producing antibodies as recited in the instant claims, including methods employing CHO cells, NS0 cells, and mice transgenic for human Ig genes. The references also supply ample motivation and evidence for expectation of success, as discussed supra.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art over the claims of copending Application USSN 10/776,649.

This is a provisional obviousness-type double patenting rejection.

21. Claims 105 – 113, 115 – 124, 126 – 135, 137 – 147, 164 – 169, 171 – 173, and 175 – 176 are rejected under the judicially created doctrine of **obviousness-type double** patenting as being unpatentable over claims 4 and 6 of U.S. Patent No. 6,682,736 in view of in view of Kucherlapati et al. (US Patent 5,939,598; of record, see entire document), Kuchroo et al. (US Patent 6,207,156; or record, see entire document), and European Patents 0 216 846 and 0 256 055 (of record, see entire documents).

U.S. Patent No. 6,682,736 claims an anti-CTLA-4 antibody which possesses selectivity for CTLA-4 over CD28, B7-2, CD44, and hIgG1 of greater than about 100:1, inhibits binding between CTLA-4 and B7-2 and between CTLA-4 and B7-1 with an IC_{50}

of lower than about 100 nM, i.e. has the same functional characteristics as the instantly claimed antibody. Therefore, it is an inherent property of the antibody claimed in the '736 Patent to compete with the instantly claimed antibody for binding to CTLA-4.

U.S. Patent No. 6,682,736 does not claim methods of producing said antibodies.

However, an ordinary artisan at the time the invention was made would immediately envisage such methods, as evidenced by the references. For example, Kucherlapati et al., Kuchroo et al., and European Patents 0 216 846 and 0 256 055 have been discussed supra, and teach the various methods of producing antibodies as recited in the instant claims, including methods employing CHO cells, NS0 cells, and mice transgenic for human Ig genes. The references also supply ample motivation and evidence for expectation of success, as discussed supra.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art over the claims of U.S. Patent No. 6,682,736.

22. Conclusion: No claim is allowed.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ILIA OUSPENSKI
Patent Examiner
Art Unit 1644

January 26, 2005

Phillip Gambel
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PRIMARY EXAMINER
TECH CENTER 1600
1/31/05